REMARKS

REJECTION UNDER 35 U.S.C. §112, SECOND PARAGRAPH

The Action rejected claims 1, 5, 12-30 under 35 U.S.C. 112 for the following reasons:

- "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
- "The distinction between a micellar dispersion and emulsion as recited in claims 1 and 29 is unclear. Micelles are emulsions since micelles of one phase are in suspension in another phase."

The applicant responds to the above rejections with the following amendments to the claims.

These amendments to claims 1, 5, 12-30 address each and every objection and/or rejection raised, for example:

1. A formulation for application to a mucosal tissue selected from the group consisting of nasal, ophthalmic, oral cavity, gastrointestinal, respiratory, vaginal and rectal, the formulation comprising

(a) a biologically active agent selected from the group consisting of antibiotic, antiviral agent, antifungal agent, disinfectant, nutrient, anti-inflammatory agent, local anesthetic and essential oil; and

(b) a lipid carrier, said lipid carrier including at least one lipid selected from the group of amphiphilic phospholipids consisting of yolk lecithin, soya lecithin, phosphatidylglycerol and [analogs thereof] phosphatidylcholine, said lipid being characterized as [a colloidal micellar dispersion or as] an emulsion of lipid

droplets dispersed in an aqueous medium, and said lipid and said biologically active agent being present in a ration of from about 10:1 to about 1:10, such that said biologically active agent is carried bys aid lipid of said lipid carrier and said biologically active agent is thereby released from said lipid in a sustained manner and over a prolonged period of time [when compared to the same formulation without said at least one lipid and], such that said lipid carrier has a property of high adhesion to the mucosal tissue.

5. The formulation of claim 1, wherein said disinfectant is selected from the group consisting of chlorhexidine [and salts thereof], chlorhexidine salts, triclosan, cetrimide, and cetylpyridinium chloride.

12. The formulation of claim 1, wherein said biologically active agent is further characterized by having activity in the oral cavity, said activity being suitable for treatment of at least one condition selected from the group consisting of gum disease, caries, dry mouth, malodorous breath, and microbial infection.

13. The formulation of claim 12, wherein said microbial infection [includes an infection] is selected from the group consisting of bacterial, viral and fungal.

14. The formulation of claim 1, wherein said biologically active agent is further characterized by having activity on a tissue selected from the group consisting of nasal, ophthalmic, vicinal, and rectal, said activity being suitable for treatment of at least one condition selected from the group consisting of inflammation, irritation, dryness and microbial infection.

15. The formulation of claim 14, wherein said microbial infection [includes an infection] is selected from the group consisting of bacterial, viral and fungal.

16. The formulation of claim 1, wherein said lipid in (b) and said biologically active agent in (a) are present in a ratio of from about 5:1 to about 1:5.

17. Claim 17 depends on claim 16, as amended above.

18. The formulation of claim 1, further comprising a stabilizer, said stabilizer [including] having at least one surfactant selected from the group consisting of non-ionic, anionic, cationic and amphiphilic.

19. The formulation of claim 18, wherein said [stabilizer is] non-ionic surfactant is selected from the group consisting of a polyethylene glycol derivative[s] and a glycerol derivative[s].

20 The formulation of claim 19, wherein said polyethylene glycol derivative is selected from the group consisting of Tween[s], triton[s], tyloxapol, pluronic[s], Brije[s], Span[s], poloxamer[s] and emulphor[s].

21. The formulation of claim 19, wherein said glycerol derivative is selected from the group consisting of polyglycerine[s] and polyalkylglyceride[s].

22. The formulation of claim 18, wherein said [stabilizer is an] anionic surfactant is selected form the group consisting of carboxylate[s], alkyl sulfonate, aryl sulphonate[s] and phosphate[s].

23. The formulation of claim 18 wherein said [stabilizer is a] cationic surfactant is selected from the group consisting of alkyl pyridinium salt and tetra-alkylammonium salt.

24. The formulation of claim 18, wherein said [stabilizer is an] amphiphilic surfactant is selected form the group consisting of alkyl betaine derivative[s], cocoamphodiacetale derivative[s], lauroamphoacetate[s] and phosphatidylglycerol.

25. The formulation of claim 1, further comprising at least one lipid additive selected from the group consisting of triglyceride[s], alkyl ester[s], cholesterol, triolein, edible oil[s], medium chain glycerate[s], isopropylmyristate and cholesterol ester[s].

26. The formulation of claim 1, further comprising at least one additive selected from the group consisting of flavor[s], aroma modifier[s], sweetener[s], color[s], and antioxidant[s].

27. Claim 27 depends on amended claim 26.

28. The formulation of claim 1, wherein said lipid is in the form of a[n] dispersion having lipid particles of size in the range of from about 50 to about [500] 300 nm.

29. A method of administering a formulation to a mucosal tissue, wherein said mucosal tissue is selected from the group consisting of nasal, ophthalmic, oral cavity, gastrointestinal, respiratory, vaginal and rectal, comprising the steps of

(a) providing the formulation, the formulation featuring

(i) a biologically active agent selected from the group consisting of antibiotic, antiviral agent, antifungal agent, disinfectant, nutrient, anti-inflammatory agent, local anesthetic and essential oil; and

(ii) a lipid carrier, said lipid carrier including at least one lipid selected from the group of amphiphilic phospholipids consisting of yolk lecithin, Soya lecithin, phosphatidylglycerol and [analogs thereof]

phosphatidylcholine, said lipid being characterized as [a colloidal micellar dispersion or as] an emulsion of lipid droplets dispersed in an aqueous medium, and said lipid and said biologically active agent being present in a ration of from about 10:1 to about 1:10, such that said biologically active agent is carried bys aid lipid of said lipid carrier and said biologically active agent is thereby released from said lipid in a sustained manner and over a prolonged period of time [when compared to the same formulation without said at least one lipid and], such that said lipid carrier has a property of high adhesion to the mucosal tissue; and

(b) administering the formulation to the mucosal tissue.

30. Claim 30 depends on amended claim 29.

Therefore, all of the informalities corrected above overcome the rejections under Section 112, second paragraph.

REJECTION UNDER 35 U.S.C. §102(b)

The Action rejects claims 1, 12-18, 25, 26, 28-30 under 35 U.S.C. 102(b) as being anticipated by WO 88/00824 because the action states that WO discloses liposomal formulations for mucosal application which contain egg lecithin and antibiotics.

In response, the applicants disagree with the Action because to anticipate a claim, the reference must teach every element of the claim (MPEP 2131). Patent WO 88/00824 teaches, as an essential element, "positively charged lipid components," used in preparing the liposomes of the invention (specification p. 10). The reference goes on to limit the amount of lipid components with a negative charge (page 22 of specification) because such components would reduce the positive charge of the lipid components, thereby reducing the effectiveness of the invention. The present invention does not require lipids of a positive charge and is therefore not anticipated by WO. In fact, the present invention teaches away from the cited reference and therefore, the above rejection should be withdrawn.

The Action also rejects claims 1, 12-18, 25, 26, 28-30 under 35 U.S.C. 102(b) as being anticipated by Amselem (US Patent No. 5,662,932) because the Action states "Amselem discloses nanoemulsions containing antifungal agent, miconazole, egg lecithin, tricaprin, cholesterol, oleic acid and tocopherol succinate. The drug:lipid ratios fall within the claimed ratios. The composition further contains surfactants such as Tweens. The modes of administration are oral, rectal and nasal."

In response, the applicants disagree with the Action because it does not teach every element of the present invention. Amselem (US Patent No 5,662,932)

recites in claim one as an essential element, a "lipid core surrounded by at least one phospholipid bilayer" envelope. The present invention does not require a phospholipid envelope. Amselem does not teach a formulation which does not include a phospholipid envelope, so the present invention is not anticipated, and the above rejection should be withdrawn.

REJECTION UNDER 35 U.S.C.102(e)

The Action also rejects claims 1, 5, and 12-30 under 35 U.S.C. 102(e) as being anticipated by Schwartz (US Patent No. 6,117,415). The Action states that Schwartz discloses oil in water emulsions containing either chlorhexidine or triclosan, egg lecithin, triglyceride, alpha-tocopherol hemisuccinate, Tween, peppermint oil, as well as the other claimed surfactants. The particle sizes in Schwartz are 250 nm to 350 nm.

In response, the applicants disagree with the Action. Schwartz (US Patent No 6,117,415) has as an essential element in claim one a bioadhesive polymer coating on each submicron particle of lipid. The bioadhesive polymer coating "leads to significant prolongation of the drug presence on the mucous surfaces of the mouth." (col. 2, lines 20-23). The present invention does not have such a coating as an essential element, and therefore is not anticipated by the reference because the reference does not teach every element of the present invention. Therefore, the above rejection should be withdrawn.

REJECTION UNDER 35 U.S.C. 103(a)

The Action rejects claims 1, 12-18, 25, 26, 28-30 under 35 U.S.C. 103(a) as unpatentable over WO 88/00824 because although WO does not teach the entire claimed range of lipid to active agent, it is obvious to one skilled in the art to vary the amount of active agents from the amounts in WO since the amounts of active agents to be administered depend on the condition of the disease and other factors.

In response, the applicant disagrees with the Action. "A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention." (MPEP 2141.02). Patent WO 88/00824 teaches as an essential element in claim 1, positively charged vesicle forming lipid components, and as stated above, limits the amount of negatively charged lipid components so that the positive charge is not reduced. WO teaches away from the present invention. The present invention teaches, contrary to the reference, the use of amphiphilic phospholipids; the present invention does not require a positively charged lipid component therefore, as a matter of fact and law, the above rejection cannot be upheld.

The Action rejects claims 1, 12-20, 22, 24-30 under 35 U.S.C. 103(a) as being unpatentable over Amselem (US Patent No 5, 662, 932) because although Amselem does not teach the entire claimed range of lipid to active agent, it is obvious to one skilled in the art to vary the amount of active agents from the amounts in Amselem since the amounts of active agents to be administered depend on the condition of the disease and other factors

In response, the applicant disagrees with the Action. The claimed invention as a whole would not have been obvious in light of Amselem because the reference teaches a lipid core with a phospholipid envelope as an essential element, but no such envelope is required in the present invention. (MPEP 2141.02). Therefore, as a matter of fact and law, the above rejection cannot be upheld.

The Action rejects claims 1, 5, 12-30 under 35 U.S.C. 103(a) as being unpatentable over Schwarz because it would be obvious to one of ordinary skill in the art to vary the active agent amounts from the guidance provided by Schwarz, since the amounts of active agents to be administered depend on the condition of the disease and other factors.

In response, the applicant disagrees with the Action. The claimed invention as a whole would not be obvious in light of Schwartz. Schwarz has as an essential element a bioadhesive polymer coating on lipid particles which is necessary for adherence to mucosal membranes. The lipids of the present invention do not have a bioadhesive coating necessary to adhere to mucosal membranes, so the present invention is not obvious in light of Schwarz. Therefore, as a matter of fact and law, the above rejection cannot be upheld.

Therefore, claims 1, 5, 12-30 are in condition for allowance and notice to that effect is earnestly solicited. If, for any reason, the Examiner should deem that this application is not in condition for allowance, the Examiner is respectfully requested to telephone the undersigned attorney to resolve any outstanding issues.

Respectfully submitted:

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According to another preferred embodiment of the present invention, the formulation preferably also includes at least one lipid additive selected from the group consisting of triglycerides, alkyl esters, cholesterol, triolein, [Soya oil], edible oils, medium chain glycerides, isopropylmyristate and cholesterol esters.

MARKED UP COPY OF CLAIM AMENDMENTS UNDER 37 C.F.R. 1.121

1. (Amended) A formulation for application to a mucosal tissue selected from the group consisting of nasal, ophthalmic, oral cavity, gastrointestinal, respiratory, vaginal and rectal, the formulation comprising

(a) a biologically active agent selected from the group consisting of antibiotic, antiviral agent, antifungal agent, disinfectant, nutrient, anti-inflammatory agent, local anesthetic and essential oil; and

(b) a lipid carrier, said lipid carrier including at least one lipid selected from the group of amphiphilic phospholipids consisting of yolk lecithin, soya lecithin, phosphatidylglycerol and [analogs thereof] phosphatidylcholine, said lipid being characterized as [a colloidal micellar dispersion or as] an emulsion of lipid droplets dispersed in an aqueous medium, and said lipid and said biologically active agent being present in a ration of from about 10:1 to about 1:10, such that said biologically active agent is carried by said lipid of said lipid carrier and said biologically active agent is thereby released from said lipid in a sustained manner and over a prolonged period of time [when compared to the same formulation without said at least one lipid and], such that said lipid carrier has a property of high adhesion to the mucosal tissue.

5. (Amended) The formulation of claim 1, wherein said disinfectant is selected from the group consisting of chlorhexidine [and salts thereof], chlorhexidine salts, triclosan, cetrimide, and cetylpyridinium chloride.

12. (Amended) The formulation of claim 1, wherein said biologically active agent is further characterized by having activity in the oral cavity, said activity being suitable for treatment of at least one condition selected from the group consisting of gum disease, caries, dry mouth, malodorous breath, and microbial infection.

13. (Amended) The formulation of claim 12, wherein said microbial infection [includes an infection] is selected from the group consisting of bacterial, viral and fungal.

14. (Amended) The formulation of claim 1, wherein said biologically active agent is further characterized by having activity on a tissue selected from the group consisting of nasal, ophthalmic, vicinal, and rectal, said activity being suitable for treatment of at least one condition selected from the group consisting of inflammation, irritation, dryness and microbial infection.

15. (Amended) The formulation of claim 14, wherein said microbial infection [includes an infection] is selected from the group consisting of bacterial, viral and fungal.

16. (Amended) The formulation of claim 1, wherein said lipid in (b) and said biologically active agent in (a) are present in a ratio of from about 5:1 to about 1:5.

17. Claim 17 depends on claim 16, as amended above.

18. (Amended) The formulation of claim 1, further comprising a stabilizer, said stabilizer [including] having at least one surfactant selected from the group consisting of non-ionic, anionic, cationic and amphiphilic.

19. (Amended) The formulation of claim 18, wherein said [stabilizer is] non-ionic surfactant is selected from the group consisting of a polyethylene glycol derivative[s] and a glycerol derivative[s].

20. (Amended) The formulation of claim 19, wherein said polyethylene glycol derivative is selected from the group consisting of Tween[s], triton[s], tyloxapol, pluronic[s], Brije[s], Span[s], poloxamer[s] and emulphor[s].

21. (Amended) The formulation of claim 19, wherein said glycerol derivative is selected from the group consisting of polyglycerine[s] and polyalkylglyceride[s].

22. (Amended) The formulation of claim 18, wherein said [stabilizer is an] anionic surfactant is selected form the group consisting of carboxylate[s], alkyl sulfonate, aryl sulphonate[s] and phosphate[s].

23. (Amended) The formulation of claim 18 wherein said [stabilizer is a] cationic surfactant is selected from the group consisting of alkyl pyridinium salt and tetra-alkylammonium salt.

24. (Amended) The formulation of claim 18, wherein said [stabilizer is an] amphiphilic surfactant is selected form the group consisting of alkyl betaine derivative[s], cocoamphodiacetale derivative[s], lauroamphoacetate[s] and phosphatidylglycerol.

25. (Amended) The formulation of claim 1, further comprising at least one lipid additive selected from the group consisting of triglyceride[s], alkyl ester[s], cholesterol, triolein, edible oil[s], medium chain glycerate[s], isopropylmyristate and cholesterol ester[s].

26. (Amended) The formulation of claim 1, further comprising at least one additive selected from the group consisting of flavor[s], aroma modifier[s], sweetener[s], color[s], and antioxidant[s].

27. Claim 27 depends on amended claim 26.

28. (Amended) The formulation of claim 1, wherein said lipid is in the form of a[n] dispersion having lipid particles of size in the range of from about 50 to about [500] 300 nm.

29. (Amended) A method of administering a formulation to a mucosal tissue, wherein said mucosal tissue is selected from the group consisting of nasal, ophthalmic, oral cavity, gastrointestinal, respiratory, vaginal and rectal, comprising the steps of

(a) providing the formulation, the formulation featuring

(i) a biologically active agent selected from the group consisting of antibiotic, antiviral agent, antifungal agent, disinfectant, nutrient, anti-inflammatory agent, local anesthetic and essential oil; and

(ii) a lipid carrier, said lipid carrier including at least one lipid selected from the group of amphiphilic phospholipids consisting of yolk lecithin, Soya lecithin, phosphatidylglycerol and [analogs thereof] phosphatidylcholine, said lipid being characterized as [a colloidal micellar dispersion or as] an emulsion of lipid droplets dispersed in an aqueous medium, and said lipid and said biologically active agent being present in a ration of from about 10:1 to about 1:10, such that said biologically active agent is carried bys aid lipid of said lipid carrier and said biologically active agent is thereby released from said lipid in a sustained manner and over a prolonged period of time [when compared to the same formulation without said at least one lipid and], such that said lipid carrier has a property of high adhesion to the mucosal tissue; and

(b) administering the formulation to the mucosal tissue.

30. Claim 30 depends on amended claim 29.